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From: Kathryn Guyton
Sent: Mon 11/24/2014 5:58:48 PM
Subject: IARC monograph vol 112-- examples

Hi everyone,

Thanks again to all for the great discussion last week. We greatly appreciate your contributions!

As promised, I have posted some example Section 4s from the volume 110 IARC monograph here: http://iops.iarc.fr/index.php?page=proj_files&project_id=118 (login required). This is selected text, figures and tables from the meeting drafts, not for distribution. While the text gives an idea of the level of detail and writing style, the volume 112 outline is quite different and you should consult what is posted here http://iops.iarc.fr/index.php?page=project&project_id=118.

In general Section 4 provides statements of fact; avoid “the authors concluded..”, instead giving the opinions of the Working Group in square brackets, e.g., [The Working Group notes that these data indicate an anti-proliferative response]. Please also see additional comments for each of you below.

Don't hesitate with questions or requests as you move forward with your writing assignments.

Best,
Kate

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Section 4.1 **Matt Ross**— it's fine to change the outline structure to ADME (and within each, human then experimental systems) as is done in these examples. The writing style exhibited here would be just

wonderful: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3569858/> :-).

Section 4.2 **Frank**— bonjour! It would be great to organise this section into the following subheadings: DNA damage; mutation; chromosomal aberrations; DNA repair; cell transformation; within each, human, animal, other species. I'll send you some ideas on which assays may best fit where, and example table formats for each.

Section 4.3 and 4.4— **Ivan, Lauren and Matt M.** These sections have been most significantly reorganised around the 10 characteristics of carcinogens, and is divided among you. Within your assigned topics, you CAN structure the text by target organ if it makes sense to do so, but it isn't necessary. Often Sections 2 and 3 will seek input from Section 4 on the mechanisms relevant to observed tumour findings. Regarding the cancer target organs: the epidemiology sections are all considering leukaemia/lymphoma as a potential cancer endpoint, among others; I can inform you these and of the animal bioassay target organs.

Matt Martin— this is the level of detail desired for 4.5 Other adverse effects:

1,2-Dichloropropane causes hepatic and renal toxicity, including fatty degeneration and necrosis, in both humans (Perbellini *et al.*, 1985; Pozzi *et al.*, 1985; Lucantoni *et al.*, 1992; Fiaccadori *et al.*, 2003) and experimental systems (Heppel *et al.*, 1946, 1948; NTP, 1986). Damage is often extensive, and sometimes fatal. Haemolytic anaemia as a result of 1,2-dichloropropane exposure has also been consistently reported across human and experimental animal studies (Heppel *et al.*, 1946; Pozzi *et al.*, 1985; Lucantoni *et al.*, 1992; Umeda *et al.*, 2010; Matsumoto *et al.*, 2013). Nasal, but not lung, toxicity has been reported in mice and rats exposed to 1,2-dichloropropane via inhalation, with effects observed including desquamation of the olfactory epithelium (Umeda *et al.*, 2010; Matsumoto *et al.*, 2013).

The liver is the most prominent target tissue of PFOA, with rats and mice being the most responsive species to liver effects. Limited data are available indicating liver toxicity in non-human primates (Butenhoff *et al.*, 2002). Additionally, serum levels of PFOA have been positively associated with serum markers of liver injury in humans (Sakr *et al.*, 2007; Lin *et al.*, 2010; Gallo *et al.*, 2012). Prenatal and early life exposures to PFOA also affect mammary gland development in rodents.

Ivan— this is the level of detail desired for 4.4 Cancer susceptibility data, unless there are studies with cancer as an endpoint. :-) But you can also mention any relevant data that would impact the evaluation:

No direct data on susceptibility were available to the Working Group.

Matt M. and Ivan— see Section 4.3.8 in the PFOA example regarding the ToxCast/Tox21 assays, suggest this length of text supplemented as needed to describe your planned analyses.

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